

Variability of Blood Lead Concentrations During Infancy

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ABSTRACT. As part of a study of early childhood development, more than 200 children had their blood lead concentrations (PbB) determined semiannually during the first 2 yr of life. These children were selected from 11,837 consecutive births surveyed for umbilical cord PbB at Boston Lying-In Hospital. Candidate subjects were drawn from the highest, lowest, and middle deciles of PbB. The mean PbB was 7.2 ± 5.3 (standard deviation) $\mu\text{g/dl}$ at birth and did not change appreciably with age. However, the average change in an individual's PbB every 6 months was $4 \mu\text{g/dl}$, which was several fold in excess of the analytical reproducibility. Only 25% of the children in the highest category at birth were in the highest category at 2 yr of age. Approximately 40% of the children remained in their immediately previous PbB tertile category. A stochastic description of these patterns of change fits the data. Our results should caution investigators who might wish to rely on a single determination to categorize children with PbB.

THE CONCENTRATION OF LEAD in blood (PbB) has become a widely used index of body or target organ burden of lead. As such, PbB has been used to diagnose lead intoxication and to gauge exposure in epidemiological, field, and laboratory studies of lead's toxic effects. The utility of PbB is enhanced by its persistence. In the presence of constant, ambient exposure, PbB does not fluctuate markedly in the adult. The turnover time of lead atoms in blood is approximately 1 month in men,¹ and abrupt changes in occupational exposure are accompanied by PbB changes with a time constant of about 1 month.²

Presently, however, the situation in children is less clear. Their kinetics are not as well studied, but because of children's higher fractional gut absorption rates, more active bone growth, and smaller mass, it may be assumed that their kinetics are the same or slightly faster than adults. The monthly stability of PbB in a cohort of 29 hyperactive/learning-disabled 4- to 12-yr-olds has been reported by David et al.³ to be "of a reasonably high order," with Pearson correlation coefficients of 0.7-0.8. This implies only fairly steady metabolic fluxes of lead, as well as nearly constant exposure and intake.

We report herein our observations of PbB in a group of 200 infants monitored from birth to 2 yr of age. Both individual and group changes in PbB with aging are examined.

METHODS

Umbilical cord specimens were collected and measured in duplicate from 11,837 consecutive births at the Boston Lying-In (now Brigham and Women's) Hospital between June, 1979 and April, 1981. This hospital serves a geographically and demographically diverse population. The survey of cord PbB was used to generate a list of candidate subjects for a study of the developmental effects of in utero lead exposure. To be eligible for inclusion in this study, the newborn must have had a PbB in the highest, lowest, or middle decile; been free of medical conditions which required a hospital stay of more than a few days; and been expected to reside in an English-speaking household within 10 miles of the hospital for the 2 yr that followed.

Details of the analytical procedure have been reported previously.⁴ Umbilical cord whole blood specimens were sonicated, acid digested in a microwave oven, and then assessed by anodic stripping voltametry (ESA Model 2014, Bedford, MA). The 6-, 12-, 18-, and 24-month specimens were collected in capillary tubes by trained technicians. Extensive skin preparation with alcohol scrubs were employed to minimize sample contamination with lead. These

Table 1.—Blood Lead Levels at Different Ages among Children Classified by Cord Blood Lead

Age	Cord Blood Lead Category			Overall
	Low (N = 74)	Middle (N = 74)	High (N = 67)	
Birth	1.8 (0.7)*	6.6 (0.6)	14.0 (3.4)	7.2 (5.3)
6 mo.	4.4 (3.9)	7.0 (7.8)	6.9 (8.6)	6.2 (7.1)
12 mo.	6.1 (5.2)	8.6 (7.6)	8.3 (6.2)	7.7 (6.5)
18 mo.	6.5 (5.6)	8.5 (5.9)	7.1 (6.4)	7.6 (5.7)
24 mo.	5.6 (4.9)	7.2 (5.0)	7.3 (8.2)	6.8 (6.3)

* $\mu\text{g}/\text{dl}$, mean (standard deviation).

samples were assayed in duplicate or triplicate with a model 3010 anodic stripping voltameter utilizing an exchange reagent. The analytical system was calibrated with aqueous standards of known lead concentrations. No interference from varying copper concentrations was observed. Each batch of samples was accompanied by blood samples of known lead concentrations to quantify intralaboratory variability. In addition, several standardized blood samples with lead concentrations measured to three significant figures by isotope

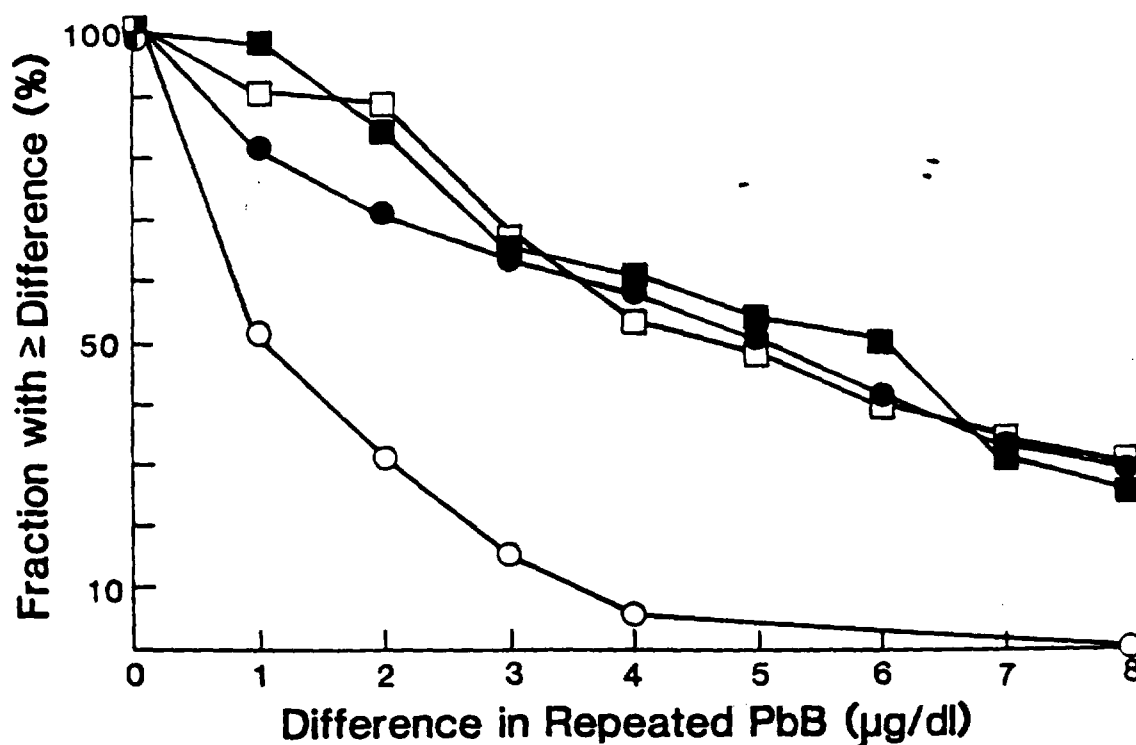


Fig. 1. Relative occurrences of blood lead changes. Differences between repeated measurements at intervals of 6 months, 1 yr, and 2 yr are shown in the upper curves. The lower curve shows differences seen for samples collected on the same day from a child. Fluctuations in blood lead exceed analytical artifacts to the extent that the upper curves exceed the lower curve.

dilution mass spectrometry were also included after they become available in 1982 from the Centers for Disease Control.

RESULTS

The observed cord PbB in the larger population has been described elsewhere.⁴ A prominent seasonal pattern is superimposed on a general declining trend. Particular characteristics of individual mothers were associated in general with significantly different PbB: older maternal age and tobacco, coffee, and alcohol use were associated with elevated cord blood lead levels, and increased parity was associated with lower lead levels.⁵

The mean PbB values for the smaller group of infants selected for longitudinal study did not decline over time (Table 1). The number of subjects participating in the study decreased during the 2 yr primarily because of families moving. Approximately 10% of the subjects were lost to follow-up blood sampling each year. The mean PbB of this cohort did not change significantly during the 2 yr (Table 1).

Other shifts in PbB associated with maturation were sought. The change in PbB during each 6-month interval was calculated (Δ PbB) for each subject. The Δ PbB does not depart from zero, which indicates that PbB as a whole does not systematically change with age in this group.

One measure of individual variability is the change with time in the absolute value of Δ PbB. The average value of this change was approximately 5 μ g/dl, regardless of whether a 6-month, 1-yr, or 2-yr interval was represented (Fig. 1). Changes in PbB as much as 8 μ g/dl were observed 20% of the time. These changes far exceed the difference in PbB observed when duplicate samples from the same child are measured on the same day (lowest curve in Fig. 1). Pairs of samples collected from a child on the same day differed by approximately 1 μ g/dl; differences as large as 4 μ g/dl were detected less than 10% of the time. The changes seen in a child over time, therefore, are not due solely to analytical artifacts.

The probabilities that a child remains in his tertile or changes tertiles at the time of the next measurement are displayed as "transitional matrices" (Table 2). A minimum of 38% are concordant from one measurement to the next. Indeed, fully 38% are concordant on the birth and 2-yr measurements.

During the first year, 21% of the children moved from one extreme tertile (i.e., either the lowest or highest) to the other extreme. During the second year, however, an appreciably smaller fraction of children rose or fell two tertiles. Between birth and 2 yr only 19% had a blood lead change that moved them two tertiles away from their original placement.

Spearman correlation coefficients of PbB at various ages increased with age (Table 3). Elevated lead levels

Table 2.—Transitional Matrices: Fraction of Children Changing PbB Categories* at Different Ages

Ages		Category Before	Category After			No. Subjects	Fraction Concordant (%)
Before	After		Low	Mid	High		
Birth	6 mo.	Low	16%	10%	8%	215	38
		Mid	12	10	11		
		High	13	9	12		
6 mo.	12 mo.	Low	13	12	14	194	40
		Mid	9	10	11		
		High	7	6	17		
12 mo.	18 mo.	Low	18	11	7	197	47
		Mid	9	11	9		
		High	6	12	19		
18 mo.	24 mo.	Low	22	9	2	198	55
		Mid	12	15	6		
		High	6	11	8		
Birth	24 mo.	Low	17	8	7	198	38
		Mid	11	13	13		
		High	12	12	8		

* Categories were defined to the nearest 0.1 μ g/dl so that each tertile (i.e., third) was equally populated at each age. The middle tertile at birth was between 4.7 and 7.0; at 6 months, 2.9 and 7.1; later ages, 4.1 and 8.4.

Table 3.—Spearman Correlation Coefficients between PbB at Various Ages (r's)

	Birth	6 mo.	12 mo.	18 mo.	24 mo.
Birth		.10	.20	.09	.19
6 mo.	.10		.19	.28	.25
12 mo.	.20	.19		.41	.36
18 mo.	.09	.28	.41		.61
24 mo.	.19	.25	.36	.61	

were also defined more strictly, not as the top tertile, but as exceeding 15 $\mu\text{g}/\text{dl}$. Of the 28 children who had elevated lead levels at 18 or 24 months, one-half had elevated levels at birth or 6 months.

DISCUSSION

In this group of approximately 200 children followed from birth to 2 yr of age, the average PbB did not change markedly with age. Within this population, however, the relative standing of most children's PbB appeared to vary randomly, which changed their relative standing with respect to PbB largely at random. These changes were large enough so that 62% of these children had a tertile ranking at 2 yr that differed from their ranking at birth. Our results should caution investigators who might wish to rely on a single determination to categorize children with PbB.

Older children with more elevated PbB have been reported to display greater stability of PbB.³ Our younger subjects show much less stability, but there is a modest trend toward increasing stability of PbB with age.

Measurements of PbB are a frequently used index of recent lead exposure. In situations of transiently elevated lead exposure, however, the biological harm

attendant to increased PbB might persist longer than the PbB elevations, if of sufficient magnitude. Other tissues would, therefore, provide more suitable biopsy materials for markers of target organ dosage. Nail, tooth, bone, and hair might be candidates of such longer-term, lead-accumulating tissues. Indeed, facial hair lead levels in men have been shown to integrate several months of PbB values.⁶ Frequently repeated blood sampling would be a useful, but normally impractical, substitute.

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